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THE DECIDUA IN THE DIAGNOSIS
OF
EXTRA-UTERINE PREGNANCY.

BY
EDWARD A. AYERS, M.D.,
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New York.

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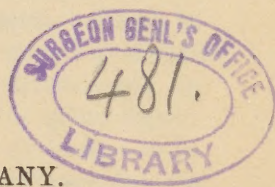
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To confirm the presence of an ectopic gestation by a safe and sure method is a pressing need. A diagnosis of gestation within the first two or even three months by clinical means can never be certain. The only sure proofs of pregnancy are the embryo, amnion, chorion, and decidua. The presence of any one of these tissues is diagnostic. In extra-uterine gestation, while the ovum and its membranes are visible only by laparotomy, yet changes generally take place in the endometrium which are practically a sure indication that the patient is pregnant. In an extra-uterine gestation the intra-uterine mucous membrane responds to the general innervation induced by fructification. Decidual formation ensues, and this change may be recognized, portions of the endometrium being removed with the curette and examined with the microscope.

The endometrium does not always change to decidua in ectopic pregnancy, hence failure to find decidual tissue does not mean the absence of pregnancy. But its presence does, un-

der certain limitations to be mentioned later. It is denied by Klein¹ that decidual cells are pathognomonic. He quotes three cases which claim the presence of decidual cells without pregnancy—one by Ruge² in endometritis, one by Leopold in dysmenorrhea, and one by Overlach in phosphorus poisoning.³

Careful investigation of these cases shows gross improbability in Klein's conclusion, and justifies our holding to the view, which is fortified by great physiological probability, that decidual cells are pathognomonic of a present or recent pregnancy. It is claimed by Klein that the flattening of the columnar epithelia lining the surface and upper portions of the utricular glands is pathognomonic of pregnancy, and that alone. He then mentions that the same change occurs, according to Hofmeier, in ichthyosis uteri and endometritis glandularis malignans, and, according to Orthmann, in salpingitis.

It is the object of this paper, first, to emphasize the view that decidual cells are pathognomonic of pregnancy, with a differentiation between a recent and a present gestation; second, that in extra-uterine pregnancy the endometrium having decidual structure can be examined, through the use of the curette, microscopically; and, third, to illustrate the different appearances of the endometrium sufficiently for diagnosis of pregnancy.

Probably no organ in the body presents microscopically such dissimilar appearances as does the mucous membrane of the uterus. Its most distinct variation appears in the normal course of events, there being practically no resemblance between a section of intermenstrual mucous membrane and fully formed decidual tissue.

Structure of Normal Mucous Membrane in the Uterus.—In Fig. 1 is shown a transverse section of the fundus uteri from a normal specimen in my collection, showing the entire mucous membrane. The proportion of space occupied by the utricular glands, and the irregularity of their arrangement, should be carefully noted. This membrane is composed chiefly of glandular epithelia, interglandular connective tis-

¹ Centralblatt für Gyn., No. 22, p. 444.

² Zeitschrift für Geburtsh. und Gyn., vol. v., 1881

³ Centralblatt für Gyn., No. 22, p. 444.

sue, and blood vessels. I quote here a brief description given in a former article :¹

“In a normal uterine mucous membrane we find, previous

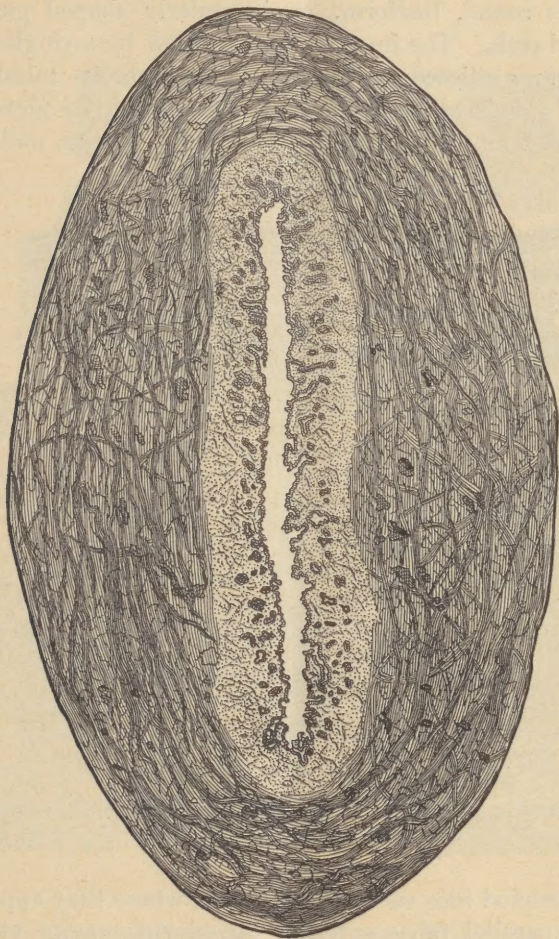


FIG. 1.—Complete transverse section of the fundus uteri, showing the entire endometrium. From a normal specimen in the author's collection.

to menstruation, the base embedded in a muscular stratum of great thickness as compared with the same in other organs. Previous to the first menstruation the middle stratum, or corium, is about one millimetre (one-twenty-fifth inch) thick.

¹ “Studies in Decidua,” New York Medical Record, April 12th, 1890.

After the first menstruation it becomes permanently about two millimetres thick. It is composed of loose vascular connective tissue containing few fibres but much structureless interfibrillar substance, and has scattered through it very numerous round, fusiform, or irregularly shaped granular nucleated cells. The inner surface is lined by a single layer of columnar ciliated epithelia. The numerous tubules or utricular glands which open into the uterine cavity pierce this layer at different angles—not as drawn by Weber, and since

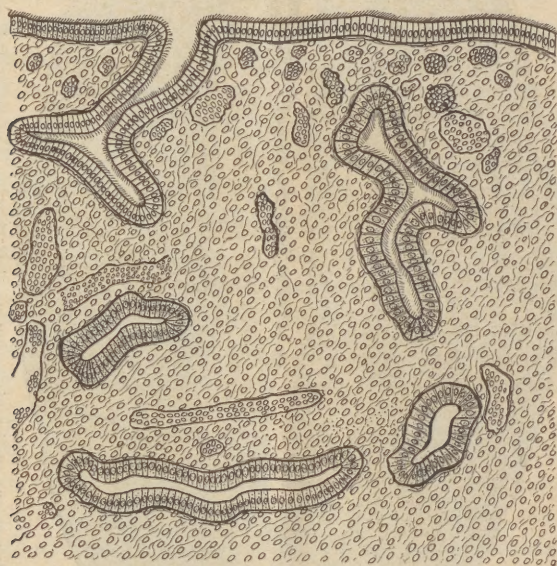


FIG. 2.—Normal endometrium. Transverse section, showing upper two-thirds.

so often copied into various text books, where they appear as straight parallel tubes entering the uterine cavity at right angles, but usually at an angle of about forty-five degrees, though the most conspicuous feature is the irregularity of their arrangement. They branch as they go deeper into the mucosa, where they are very irregularly distributed. The walls of the utricular glands are composed of a very delicate fibrillar tissue, arranged concentrically, and attached externally to the interglandular connective tissue. Internally is a single

layer of ciliated columnar epithelia, nucleated, continuous, and apparently identical in structure with the columnar epithelia lining the free surface of the uterine cavity. The epithelia in the glands are attached to one another by a trans-

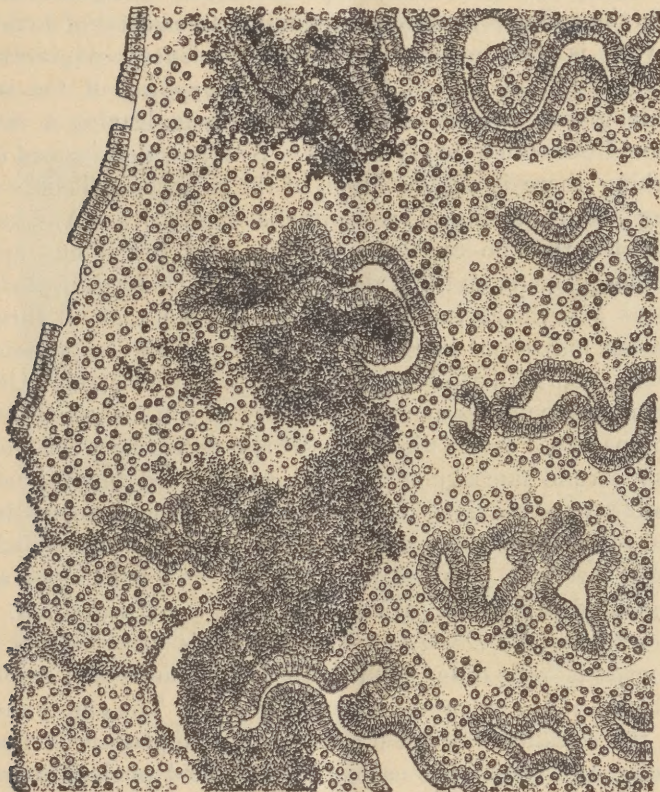


Fig. 3.—The endometrium during menstruation. (From Wyder.)

parent intercellular cement substance. They are generally uniform in shape and size."

Fig. 2 shows a portion of Fig. 1 enlarged, reproducing the upper thirds of the membrane. The relative proportions of glandular, vascular, and connective tissues should be noted, as leading to readier differential diagnosis. In Fig. 2 cilia are shown attached to the columnar epithelia; they will seldom be observed in sections.

The Mucous Membrane during Menstruation (Fig. 3).—I hesitate to introduce Wyder's illustration (Fig. 3) showing normal mucous membrane during menstruation, as I have grave doubts of its correctness.

It seems remarkable, in view of the amount of investigation the subject has received, that any and all the changes occurring in the endometrium in menstruation are matters of doubt. One view is that the endometrium experiences congestion, growth, and extravasation, followed by *sloughing* of the superficial glands, vessels, and connective tissue, leaving a raw surface from which blood exudes. Another, that instead of sloughing there is *desquamation* of the surface epithelia, exposing and rupturing the subepithelial capillaries. And last is the view that no capillaries rupture, that few if any epithelia desquamate, and that the blood is exuded by *diapedesis*. Clinical experience inclines us to the belief that all three processes may occur in the order of diapedesis; superficial desquamation with capillary rupture, and extravasation with sloughing, depending upon the severity of the menstruation. The appearance of the discharge, which varies between yellowish serum, uncoagulated blood, and clotted blood, lends plausibility to this view. Although Prof. Wyder seems inclined to the view above given, I think his illustration, made from a specimen obtained with the curette, tends to give an exaggerated part in the menstrual process to extravasation.

Structure of the Decidua.—The decidua is composed of a myxomatous reticulum filled with large embryonal cells, capillaries, and remnants of utricular glands. The embryonal cells, the so-called "decidual cells," are protoplasmic bodies, granular, and containing each a well-defined nucleus, sometimes several nuclei. The cells vary in diameter from one-seven-hundredths to one-two-hundred-and-fiftieth of an inch, or from five to fifteen times the diameter of red blood corpuscles. They have a smaller average diameter in the epicoreal decidua (reflexa) than in the other portions. Their number in a given amount of tissue also varies greatly. Generally they occupy the meshes of the myxomatous reticulum so thoroughly that under low powers of the microscope the reticulum is scarcely visible; we see only a mass of cells lying the one against its neighbors. That they do not experience compres-

sion or much consolidation is shown in their outlines, which are not square nor hexagonal, but always round or oval.

Interspersed throughout the tissue is an abundance of connective tissue and lymph corpuscles. Fig. 4 shows a section from a specimen of decidua kindly given me by my colleague, Dr. Coe. The membrane was passed from the uterus in a case of extra-uterine pregnancy of two months' gestation, the patient being successfully operated upon by Dr. Coe, who removed a specimen of tubal pregnancy. The endometrium

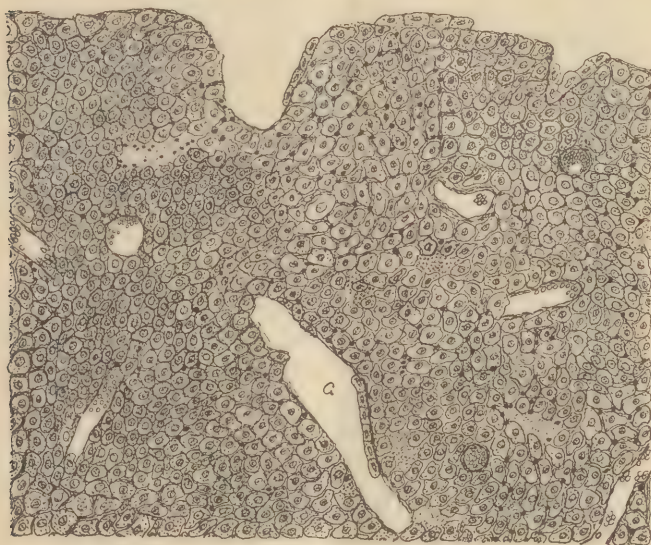


FIG. 4.—Decidua uterina, from a case of extra-uterine pregnancy.

sloughed out entire and was in good condition for microscopic examination.

Fig. 4 shows the upper third of the decidua. In this specimen the decidual cells are very large and very thick. Here and there are portions devoid of decidual cells, composed of connective tissue. Capillary vessels containing red blood corpuscles are seen. The remnant of a utricular gland is shown at G. Many of the glands have disappeared; in some specimens there are none to be seen. The relation of the utricular glands to decidual structure it seems difficult to define. Of the two views, that the decidual cell arises from

the columnar epithelia of the utricular glands (Friedländer, Frommel, Winckel) and from connective-tissue cells (Leopold, Waldeyer, Wyder, Orthmann, Heintzel, Klein), it may be said that both contribute to decidual formation. I have been incorrectly quoted by Klein¹ as restricting decidual origin to the columnar epithelia, whereas I distinctly stated that "it cannot be claimed that . . . all decidual tissue arises from the glandular epithelia."²

In the karyokinetic transformation of utricular epithelia to decidual structure, which I described, decidua occupied the connective-tissue space ere the alteration in the glands was well advanced.

It is claimed by Klein³ that the decidual cell is not pathognomonic of pregnancy, as it is found in endometritis (Ruge), in dysmenorrhea (Leopold), and in phosphorus poisoning (Overlach); and, further, that it is not present during every month of pregnancy, nor in every expelled or curetted piece of mucous membrane. Every practitioner and student must be conscious of a desire to see the exceptional conditions in which decidual cells may develop without gestation disproved. Certainly our knowledge of reproduction leading to the question of decidual cells being pathognomonic of pregnancy strongly inclines us to so consider them. The mucous membrane experiences many strong influences of blood, nerve, and lymphatic, closely bordering upon those of fructification in the sexual life, but remains the mucous membrane. But it responds with wonderful alacrity to the innervation emanating from a fructified ovum, and becomes decidua. Happily the trend of investigation tends toward this view.

We are indebted to Wyder⁴ for careful investigations of the exceptional cases mentioned by Klein. He claims that Leopold's description in a case of dysmenorrhea did not describe decidual cells, but probably large vaginal epithelia mixed with the membrane. It does not seem to have been

¹ Transactions Ger. Gyn. Society, Bonn, May, 1891; Centralblatt für Gyn., No. 22, p. 444.

² "Studies in Decidua," New York Medical Record, April 12th, 1890.

³ Centralblatt für Gyn., No. 22.

⁴ Archiv für Gyn., Heft 1-2, p. 153, 1891.

Leopold's intention to demonstrate decidual cells in dysmenorrhea, but this interpretation has been put upon his description of a specimen. In the case of Ruge, of endometritis, pregnancy had existed six years before, and was not excluded at the time the endometrium was examined. Wyder thinks the case was probably one of "chronic abortion" ("chronischen Abort") in which decidual cells remained. There can be no objection to this view. The time limits

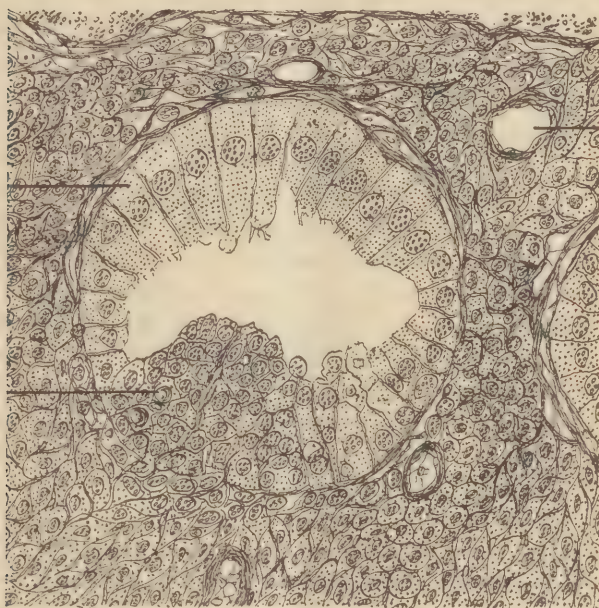


FIG. 5.—Karyokinesis of the columnar epithelia in a utricular gland.

in which decidual tissue may remain and retain some characteristic forms have not yet been defined.

In the case of Overlach, of phosphorus poisoning, the patient died in thirty-six hours, and, as Wyder very aptly remarks, "it is impossible to believe these conditions (the presence of decidual cells) developed in thirty-six hours after phosphorus poisoning."¹ His conclusion is that Overlach's patient was in a condition of "post-abortum endome-

¹ Archiv für Gyn., Heft 1-2, p. 200, 1891.

tritis" similar to that of Ruge. The paucity of cases reported, and their evident inability to withstand a careful investigation where the burden of proof is upon them, justify our believing that decidual cells arise only in pregnancy.

On the other hand, Klein holds that the flattening of the glandular and superficial epithelium is always found during pregnancy. He adds: "A conditionally similar alteration of the epithelium is found in ichthyosis uteri, but then it has at the same time several layers; also in glandular carcinoma of the body of the uterus (Hofmeier), in which markedly cuboidal or flattened superficial and glandular epithelium may be found here and there; and finally in salpingitis (Orthmann). None of these conditions, however, in connection with the other symptoms, can be mistaken for pregnancy.

"The flattening of the glandular epithelium, as is well known, affects mainly the upper portion of the glands; in their fundus, and especially where the ends of the glands project between the uppermost layers of the muscular tissue, cylindrical epithelium may persist to the termination of pregnancy; subsequently the new glandular and superficial epithelium develops from this. But where the latter might remain unchanged during pregnancy, that is, in the lowest part of the body of the uterus immediately above the internal os, it also becomes cuboidal or flattened."

I am unable to affirm or deny the correctness of these observations, as my investigations have been largely negative. In many specimens the columnar epithelia were absent, having probably been desquamated in the process of preparation.

I have described the process of karyokinesis in the columnar epithelia in a specimen of retained decidua (see Fig. 5), but there was no flattening such as is described by Klein. But we are not dependent upon this latter appearance for diagnosis.

As decidual tissue may be retained for some time following an abortion, familiarity with the appearances of such, contrasted with the decidua of ectopic pregnancy, is desirable. Most specimens of retained decidua following an abortion will show portions of the chorion or amnion, especially torn bits of villi; or if none of these tissues are present their effects

may be witnessed in the irregular surface shown by the decidua, though this would scarcely apply to the uterine decidua (vera). On the other hand, in an ectopic pregnancy the intra-uterine decidua is smooth and regular, being free from lacerations upon its free surface.

Involution of the Decidua.—In a normal pregnancy the decidua has passed its prime ere the end of the fifth month. The prominent features in the retrograde changes taking place are the transitions from decidual tissue to myxomatous and connective tissue. The decidual cells lose form, protoplas-



FIG. 6.—Involution of the decidua.

mic brilliancy, and texture on to the final stage of necrobiosis. In their stead appear the connective-tissue corpuscles. Decidual necrobiosis will also begin, following death of the ovum, either in intra- or extra-uterine pregnancy.

Following death of the ovum the decidua may recede, by a process, according to Friedländer, of "fatty degeneration," according to Klein¹ of "coagulation necrosis," to ultimate disappearance. In intra-uterine pregnancy, instead of degeneration the decidua may take on an inflammatory hyperplasia,

¹ Archiv für Gyn., 1891. Klein, "Entwicklung und Rückbildung des Decidua."

resulting in the formation of polyps, or, in conjunction with fetal membranes, of fleshy moles. Klein has given an admirable description of the decidual changes following abortion: "In a specimen four weeks after abortion round cells predominate, while islands of ill-stained, here and there barely recognizable decidual cells are still present. The latter are partly in a condition of granular disintegration, and one can see fibrous defects, the size of a decidual cell, filled only with unstained granular masses, while the fibrous framework proper is thickly sprinkled with vigorous, intensely stained round cells. The glandular epithelium, however, is chiefly but not exclusively cylindrical."

Fig. 6 is from a section of decidua uterina (vera) in my collection, in which the processes above described are almost typically shown in their transitional period. This process of involution is not dependent on death of the ovum, but naturally follows; the function of the decidua being to temporarily supply nourishment. The clinical history will generally determine the question of an abortion having occurred. An abortion may occur without the knowledge of the patient after one month's gestation, and nothing more than an excessive menstruation following one missed periodic flow be suspected. Such a history of menstrual irregularity and excess should be taken into account. If abortion occurred several months previously the curetted mucosa would show marked involution of the decidua.

In ectopic gestation the intra-uterine decidua is subject to the same laws of involution following death of the ovum; but previous to death of the ovum the process is much slower, as there is no demand upon it for nourishment. It is, however, more apt to separate *in toto* from the uterine wall before the process is far advanced. It should be borne in mind that there is no physiological obstacle to a coincident intra- and extra-uterine pregnancy.

Endometritis.—In attempting a description of the various forms of endometritis necessary for differential diagnosis of decidua, two difficulties present: First, that due to incomplete knowledge of the appearances presented; and, second, to an unsettled opinion as to classification.

Distinct types seldom prevail. Thus we speak of endo-

metritis glandularis as a hyperplasia of the utricular glands, but it would be folly to exclude the interglandular connective tissue from participation. Again, the same terms are used clinically and pathologically for different conditions, as in "membranous dysmenorrhea." Practically, for the diagnostic purposes of this article, these difficulties can be overcome.

Endometritis Glandularis.—In Fig. 7 is shown a section of

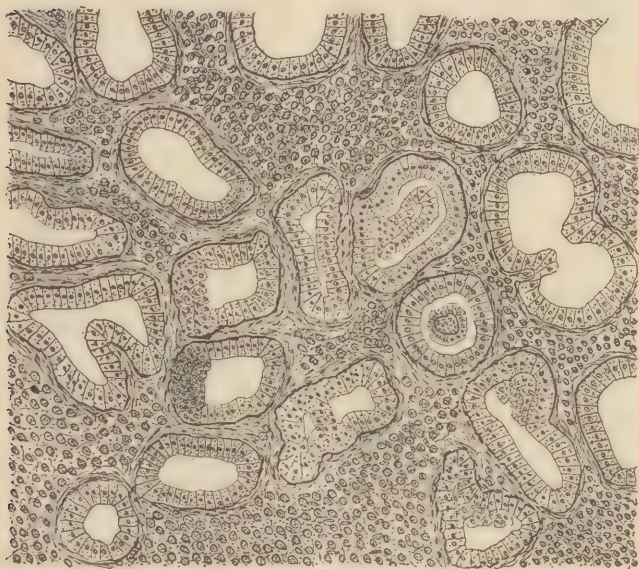


FIG. 7.—Endometritis glandularis.

the endometrium, obtained with the curette from a patient two weeks after menstruation. She gave a history of dysmenorrhea membranacea (as usually understood clinically) since puberty. Acute antelexion existed. The specimen is typical of chronic glandular endometritis. The most characteristic feature in this disease is the great increase in the amount of territory occupied by the utricular glands, with the retention of their normal appearances. The number of them appearing cut across in Fig. 7 is much greater than in

a normal specimen like Fig. 2. There is comparatively little change in the interglandular connective tissue.

There is marked thickening of the endometrium as a whole; it is much paler and somewhat softened. Catarrh accompanies this form of inflammation, and sloughing of the membrane at menstruation is liable to occur. Ruge has described a "hypertrophic" form in which there is an increase, not in the number of glands, but of the epithelia lining them.¹

Karyokinesis has been observed by Cornil² in the columnar epithelia. I have described it in other conditions, but have not observed it in this disease, but have no doubt of its occasional presence. (See Fig. 5.)

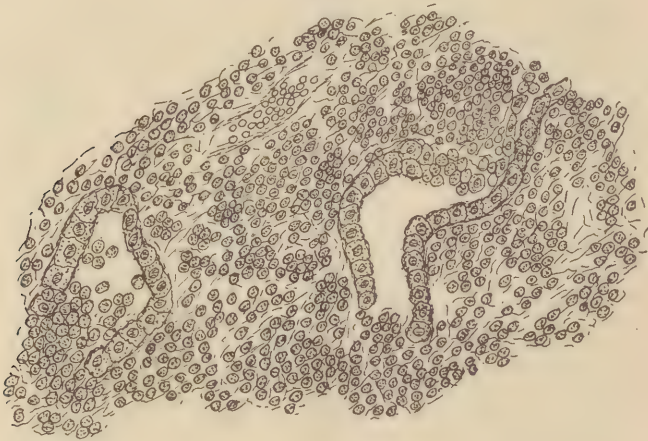


FIG. 8.—Endometritis interstitialis acuta (membranous dysmenorrhea).

Endometritis Interstitialis Acuta (membranous dysmenorrhea).—There is an unfortunate clashing of terms in the use of "membranous dysmenorrhea." Clinically it is applied to cases of painful menstruation accompanied with sloughing of more or less of the endometrium *en masse*. This clinical combination is met by more than one form of endometritis. Thus the above form of glandular endometritis would have

¹ Ruge, "Schröder's Handbuch," 9. Aufl., S. 174 u. 175.

² Cornil, "Leçons sur les Métrites," Journal des Connaissances médicales, April 21st, 1888

been classed as such. Pathologically the term has been restricted to acute interstitial endometritis superinduced upon a more or less chronic form. Mundé¹ quotes Virchow as declaring "that a deciduous membrane similar to that of pregnancy forms"—a statement utterly contrary to present

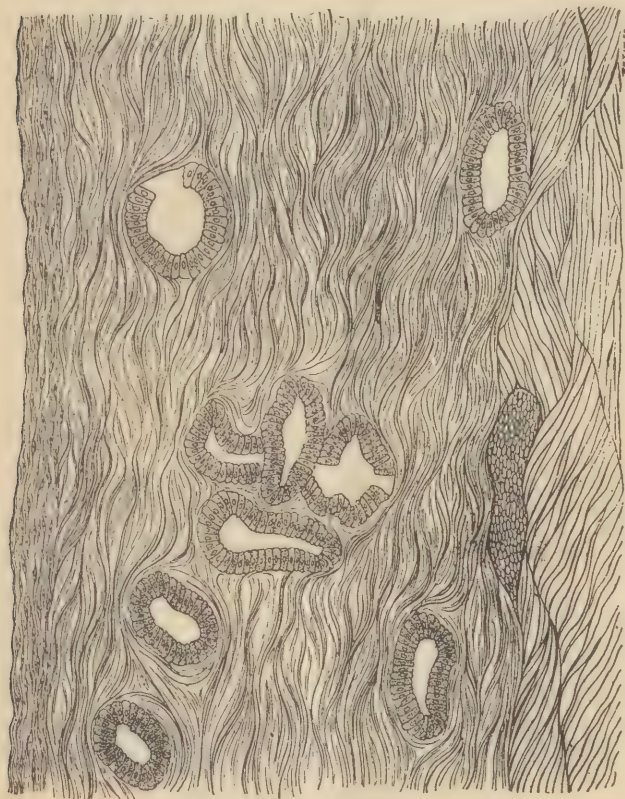


FIG. 9.—Endometritis interstitialis. Partial atrophy of the glands. (Wyder.)

knowledge, and not supported by Mundé, who further on states that "the absence of the chorionic villi and of the *large, irregular decidual cells of pregnancy* [my own italics] easily distinguishes the membrane from the decidua of pregnancy." I have already quoted Wyder's refutation of the

¹ Mundé, "Diseases of Women," Mundé and Thomas, p. 628.

statement credited to Leopold, that decidual cells were present in this form of inflammation.

The most characteristic change in the endometrium in this form is the great increase in the connective-tissue corpuscles, which become massed thickly together and show a highly

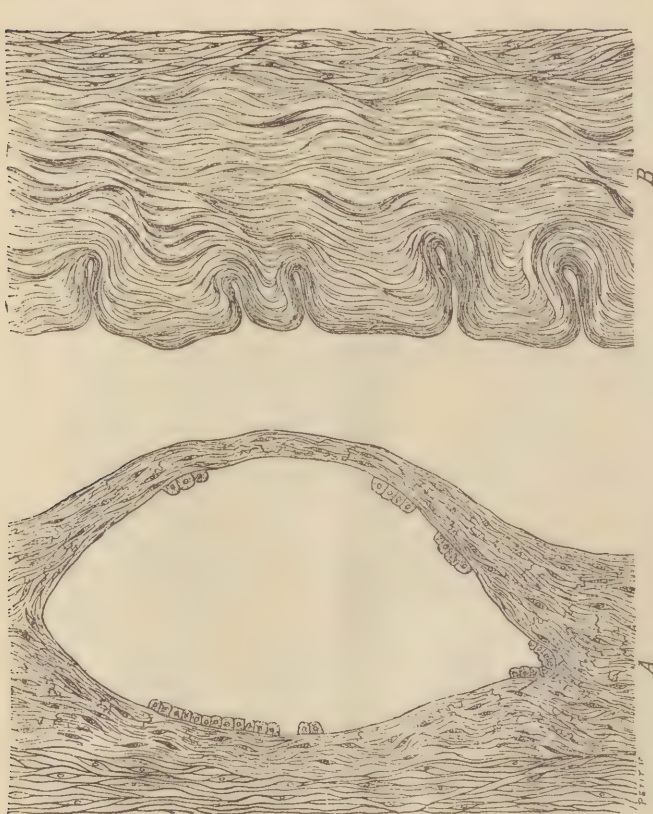


FIG. 10.—Endometritis interstitialis. Complete atrophy of the glands. A, cystic formation; last trace of glands. B, disappearance of glands. (Wyder.)

granular condition. The reticulum is less proportionately increased. The epithelia of the utricular glands lose in many cases their columnar character, become flattened and widened, or disappear. The calibre of the glands may become crowded with connective-tissue corpuscles. The glands may in places disappear. Sometimes they hypertrophy, taking on, in a slight degree, the alterations of endometritis glandularis.

Endometritis Interstitialis Chronica.—This inflammatory process results in increase of the fibrous connective tissue which lies between the glands. In proportion to the degree of this alteration is the tendency to strangulation and atrophy from compression of the utricular glands; hence the terms “endometritis interstitialis partialis” and “totalis”—names



FIG. 11.—Endometritis glandularis et interstitialis polyposa. (Wyder.)

which represent simply different degrees of the same process. The process is the formation of a true cicatricial tissue—a sclerosis. The glands, which usually slowly disappear as the sclerosis advances, may here and there dilate and form cysts. These cysts may be lined with cuboidal epithelia.

Endometritis Glandularis et Interstitialis Polyposa.—

This form of endometritis involves glandular and interstitial proliferation and inflammation, with marked tendency to cystic degeneration. The membrane is much increased in thickness, with great irregularity of surface, is soft and succulent. Vesicles varying from one to eleven millimetres in diameter may be seen upon the surface. They are glands, much distended, lined with cuboidal epithelia, degenerated columnar epithelia. These vesicles or cysts are surrounded by bands of connective tissue. Naturally the cysts are larger as they approach the surface. It is claimed by Cornil¹ that there is a penetration of the glandular tissues into the muscular base beyond the normal depth. The interglandular tissue is much altered. Spindle-shaped, nucleated cells and an increased number of connective-tissue corpuscles, more or less surrounded or embedded in a homogeneous substance, occupy the reticulum.

I omit, as not essential to the aim of this paper, a consideration of the endometrium in adenoma, carcinoma, and sarcoma. The differential diagnosis of decidua can be accomplished without it.

Summary.—1. In extra-uterine pregnancy the endometrium generally changes to decidua.

2. Decidual tissue is pathognomonic of pregnancy.

3. Portions of the endometrium may be obtained with the curette, examined with the microscope, and decidual tissue recognized if present.

4. Such tissue may be a remnant of an abortion, a part of decidua surrounding a live ovum, or due to an extra-uterine pregnancy.

5. The microscope, in connection with the clinical history, can determine to which variety the species belongs, and, if to the third, confirm the presence of an extra-uterine gestation.

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¹ Cornil, Jour. des Connaissances médicales, April-June, 1888.

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